IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMICUS THERAPEUTICS US, LLC and AMICUS THERAPEUTICS, INC., *Plaintiffs*, v. TEVA PHARMACEUTICALS USA, INC., *et al.* *Defendants*.	C.A. No. 1:22-cv-01461-CJB CONSOLIDATED

DEFENDANTS, AUROBINDO PHARMA LTD.
AND AUROBINDO PHARMA USA, INC.'S
OPENING POST-TRIAL PROPOSED FINDINGS OF FACT

TABLE OF CONTENTS

I. GENERAL 1

II. ADDITIONAL FACTS MATERIAL TO AUROBINDO'S 35 U.S.C. § 101 ARGUMENT 6

III. ADDITIONAL FACTS MATERIAL TO AUROBINDO'S 35 U.S.C. § 103 ARGUMENT 7

TABLE OF ABBREVIATIONS

Unless otherwise stated, the abbreviations below have the meanings ascribed to them in the right-hand column throughout the Defendants, Aurobindo Pharma Ltd. and Aurobindo Pharma USA, Inc.'s Opening Post-Trial Proposed Findings of Fact.

ABBREVIATION	MEANING
'388 patent	U.S. Patent No. 11,633,388 (JTX-1)
'490 patent	U.S. Patent No. 12,042,490 (JTX-2)
'164 patent	U.S. Patent No. 11,833,164 (JTX-3)
'011 patent	U.S. Patent No. 9,000,011 (DTX-14)
α-Gal A	The enzyme α-galactosidase A
POSA	Persons of ordinary skill in the art
Tr.	Trial Transcript

Aurobindo Pharma Ltd. and Aurobindo Pharma USA, Inc. (collectively, "Aurobindo"), through their undersigned counsel, hereby respectfully submit Aurobindo's Opening Post-Trial Proposed Findings of Fact as follows:

I. GENERAL

1. In the early part of 2025, Plaintiffs sold their Galafold product for $30,000 for a one-month supply of 15 150 mg migalastat hydrochloride capsules. Trial. Tr. Vol. I at 166:11-16; 168:4-13 (Mr. Keavany testifying regarding Galafold packaging and pricing).

2. At their narrowest, each of the asserted claims is directed to treating Fabry Disease patients in need by administering 150 mg of migalastat hydrochloride (or the equivalent of 123 mg migalastat free base) every other day wherein the patient has the or one among several Fabry Mutations identified in the claims. *See* JTX-1-60, JTX-1-61 (claims 8 and 36); JTX-2-JTX-2-52 (claim 9); and JTX-3-89 (claims 23-27); Trial Tr. Vol. I at 86:2-87:12; Trial Tr. Vol. I at 230:24-231:2.

3. The asserted claims from the '388 and '490 patents describe the patient in need as having the or one among several Fabry mutations identified therein as having been determined to be migalastat amenable according to an assay and amenability criteria disclosed in the patent specifications. *See* JTX 1-35 at 17:8-16 (defining "HEK Assay amenable mutations"); JTX-1-60, JTX-1-61 (claims 8 and 36); JTX-2-35 at 17:27-36 (defining "HEK Assay amenable mutations"); JTX-2-52 (claim 9); Trial Tr. Vol. I at 61:5-63:12 (Dr. Medin describing HEK Assays); Trial Tr. Vol. II at 34:16-19 (Dr. Benjamin describing HEK Assay development as directed toward "measur[ing] the response of the mutant form and its response to migalastat"), 35:7-15 (describing the R&D HEK-Assay as assessing the mutation's response to migalastat).

4. The asserted patents all cite to prior art descriptions of the claimed dosing regimen, including the Galafold product description dated May 30, 2016, and the '388 and '490 patents

detail prior art descriptions as well. JTX-1-1 (citing '011 patent at "U.S. Patent Documents" and Galafold product descriptions dating back to May 30, 2016, at "Other Publications"); JTX-1-45 at 37:60-38:13 (describing "several studies" that "investigated using 150 mg migalastat hydrochloride every other day (QOD) in Fabry patients" and determined that dosing regimen to be effective); JTX-2-41 at 29:39-58 (same); JTX-2-3 at right column (citing Galafold product descriptions dating back to May 30, 2016).

5. Plaintiffs concede that the crux of the asserted claims is the identification of specific Fabry mutations and the remainder of the claims is prior art. *See* Trial Tr. Vol. I at 25:10-21.

6. Plaintiffs' opening statement at trial included the following statement:

> So, to be clear, I want to be very clear about this, the first two parts of this, what to use for treatment and how to use it are prior art to the patents in this lawsuit. Let's make no mistake. They are prior art. The use of migalastat as a drug to treat people with responsive or amenable mutations is prior art. And how to dose them is prior art. And that, Your Honor, is where the '011 patent comes in. [The] '011 patent represents the work that was done to figure out how you should does those patients, which a very important part of this overall treatment. It's not the part that is the subject of the patents in this lawsuit. That's not the invention that we're looking at here.

Trial Tr. Vol. I at 25:10-21 (Plaintiffs' Attorney Groombridge, making opening arguments).

7. The asserted claims describe dosing methods that were well-understood and practiced by researchers in their field. *See* ¶¶ 3-5 *supra*.

8. Dr. Hopkin conceded that the dosing regimen claimed in the asserted patents is obvious. *See* Trial Tr. Vol. II at 136:16-22.

9. The methods claimed in the asserted patents each have only one step, the administration of 150 mg of migalastat hydrochloride (or 123 mg of migalastat free base equivalent) every other day. *See* JTX-1, JTX-2, JTX-3.

10. The asserted claims do not claim an assay and do not claim as a step performing an assay or evaluating assay results. *See* JTX-1, JTX-2, JTX-3.

11. The migalastat amenability criteria Plaintiffs have employed has varied over time. (*See* Trial Tr. Vol. II at 59:16-60:4 (Dr. Benjamin reading her own publication's endorsement of the precursor to the GLP-HEK Assay); Trial Tr. Vol. II at 35:23-42:22 (Dr. Benjamin discussing the Wu prior art reference (DTX-23) and noting that the results discussed therein were not definitive; discussing further assay development).

12. Before the earliest priority date for the asserted patents, it was well-known that only a limited percentage of Fabry patients could even possibly benefit from migalastat, and methods had been developed, including by Plaintiffs but also others, to try to identify mutations likely to be amenable to migalastat treatment. *See*, *e.g.*, Trial Tr. Vol. I at 132:22-134:17 (Dr. Medin addressing JTX-13, -14 and noting the authors conducted their own HEK Assays using their own amenability criteria); JTX-1-35 at 17:17-35 (describing "previous screening methods" and expressly incorporating mutations determined to be amenable using methods described in U.S. patent No. 8,592,362 ("'362 patent")); JTX-2-35 at 17:28-53 (same); JTX-3-29 at 26:12-28 (same); DTX-14-1 at abstract ("Provided are in vitro and in vivo methods for determining whether a patient with Fabry Disease will respond to treatment with a specific pharmacological chaperone"); DTX-14-16 at 13:22-14:36 (discussing "Eligibility Determination Criteria" and describing *in vitro* and *in vivo* assays for determining eligibility/amenability for pharmacological chaperone therapy); DTX-6-2 (describing migalastat as an "investigational chaperone for patients with amenable mutations"); DTX-23-1 at abstract (describing a study of a "cell-based assay in cultured HEK-293 cells" that is "a useful aid in the identification of Fabry patients with AT100 [aka migalastat hydrochloride]-responsive mutant forms"); DTX-24-2 (describing migalastat

hydrochloride as "a low molecular weight iminosugar that is orally bioavailable and that . . . target[s] α-Gal A mutants that maintain catalytic competence").

13. Plaintiffs have never publicly disclaimed any HEK Assay they have used as unreliable. *See* Trial Tr. Vol. I at 247:16-22, 256:12-257:6; Vol. II at 70:18-72:12; 73:21-24.

14. Additional Fabry mutations continue to be discovered. Trial Tr. Vol. I at 112:6-9.

15. 1-deoxygalactonojirimycin ("DGJ") and AT1001 are references to migalastat. *See* Trial Tr. Vol. I at 83:19-84:4, 121:9-12, 129:23-25; Vol. II at 41:18-19.

16. Plaintiffs' internal data showed no significant differences between the results of the GLP-HEK Assay and the R&D HEK Assay (a/k/a Clinical Trial HEK Assay). Trial Tr. Vol. I at 68:23-71:22; 145:19-146:1.

17. As new Fabry mutations are identified as amenable, Plaintiffs seek to expand the listing of mutations in their Galafold product label. *See* Trial Tr. Vol. II at 55:15-57:16 (Dr. Benjamin testifying regarding label and patent expansion).

18. The amenability determinations discussed and claimed in the asserted patents indicate only that a Fabry mutation met the inventors' criteria for amenability, and other researches employed their own amenability assays using their own amenability criteria. *See* JTX-1, JTX-2, JTX-3; *See*, *e.g.*, Trial Tr. Vol. I at 132:22-134:17 (Dr. Medin addressing JTX-13, -14 and noting the authors conducted their own HEK Assays using their own amenability criteria); JTX-1-35 at 17:17-35 (describing "previous screening methods" and expressly incorporating mutations determined to be amenable using methods described in U.S. patent No. 8,592,362 ("'362 patent")); JTX-2-35 at 17:28-53(same); JTX-3-29 at 26:12-28 (same); DTX-14-1 at abstract ("Provided are in vitro and in vivo methods for determining whether a patient with Fabry Disease will respond to treatment with a specific pharmacological chaperone"); DTX-14-16 at 13:22-14:36 (discussing

"Eligibility Determination Criteria" and describing *in vitro* and *in vivo* assays for determining eligibility/amenability for pharmacological chaperone therapy); DTX-6-2 (describing migalastat as an "investigational chaperone for patients with amenable mutations"); DTX-23-1 at abstract (describing a study of a "cell-based assay in cultured HEK-293 cells" that is "a useful aid in the identification of Fabry patients with AT100 [aka migalastat hydrochloride]-responsive mutant forms"); DTX-24-2 (describing migalastat hydrochloride as "a low molecular weight iminosugar that is orally bioavailable and that . . . target[s] α-Gal A mutants that maintain catalytic competence").

19. Plaintiffs utilized the R&D HEK Assay for enrollment in clinical trials even after FDA recommended against it. *See* Trial Tr. Vol. II at 15:19-16:7; 42:20-44:4.

20. Missense mutations are more likely to be migalastat amenable, and approximately 60% of missense mutations tested have been found to be migalastat amenable. Trial Tr. Vol. I at 76:1-78:4, 78:19-80:22; 246:2-9; Vol. II at 28:21-29:3.

21. Looking at DTX-189-9, Dr. Castelli testified that four mutations out of the 25 identified in the bottom row changed from being nonamenable to being amenable. Trial Tr. Vol. I at 209:5-14.

22. Dr. Castelli testified that the Phase III clinical trial failure was Amicus's own failure. Trial Tr. Vol. I at 234:3-11.

23. Dr. Castelli testified that he did not think it unethical to use the R&D HEK Assay even thought it did not follow Good Laboratory Practices "based on what we believed of the assay." Trial Tr. Vol. I at 234:12-235:14.

24. Four of the mutations claimed in the '388 and '490 patents were non-amenable under the R&D HEK Assay and amenable under the GLP-HEK Assay and would not have been part of the phase III clinical study that failed. Trial Tr. Vol. I at 239:6-17.

25. The sole purpose of the GLP-HEK Assay is to identify Fabry patients amenable to 150 mg of migalastat hydrochloride. Trial Tr. Vol. I at 253:6-8.

26. The dosing regimen claimed in the asserted patents had been approved for marketing in Europe in 2016 as the optimal dosing regimen for migalastat.

27. Following the failed Phase III clinical trial, Amicus simply removed patients from the study to get better results. Trial Tr. Vol. II at 125:17-126:23.

28. Following the failed Phase III clinical trial, 25 mutations went from non-amenable to amenable, but those mutations were not in the clinical trial to begin with, and only four of the 25 mutations are claimed in the asserted claims, including mutation I242F. Trial Tr. Vol. II at 126:24-132:16.

29. Dr. Hopkin testified that, regardless of whether the percentage of missense mutations was 60% or 40% or lower, he would order any mutation not identified as amenable to be tested for amenability if a test was available. Trial Tr. Vol. II at 138:12-139:13, 144:22-147:5.

II. ADDITIONAL FACTS MATERIAL TO AUROBINDO'S 35 U.S.C. § 101 ARGUMENT

30. Plaintiffs concede that the fact that humans have Fabry mutations is a natural phenomenon. Trial Tr. Vol. III at 117:17-20.

31. Plaintiffs concede the GLP-HEK Assay is integral to the inventions claimed in the '388 and '490 patents. *See* Trial Tr. Vol. I at 253:9-16.

32. The asserted claims are directed to the natural laws of Fabry mutation formation and evolution and migalastat amenability. *See* Trial Tr. Vol. I at 257:10-258:16; 262:4-263:21.

33. Nothing in the asserted claims transforms the natural laws to which the asserted claims are directed into a patentable invention.

III. ADDITIONAL FACTS MATERIAL TO AUROBINDO'S 35 U.S.C. § 103 ARGUMENT

34. According to Plaintiffs' definition, a POSA would not necessarily be familiar with the details of any HEK Assay. Trial Tr. Vol. II at 132:21-134:5.

35. A POSA would have familiarity with metabolic disorders such as Fabry Disease and can include, for example, pharmaceutical chemists and physicians. They would be expected to have attained a high degree of education and would have earned either a Master's degree, Ph.D. or M.D., followed by several years of experience in the field. They would understand biochemical principles and have a high level of skill in the area of lysosomal diseases. The POSA would work as part of a collaborative team involved in drug formulation and clinical trial writing that would include multiple POSAs with expertise in various disciplines. And, they would be aware of the literature in the art, which is limited. *See* Trial Tr. Vol. I at 54:2-55:10 (Dr. Medin testifying regarding POSA qualifications).

36. Prior to May 2017, a POSA would have been familiar with Fabry Disease, which was decoded in the 1970s by researcher Dr. Roscoe Brady. A POSA would have known that primary manifestations of Fabry Disease include a buildup of substrate in the vascular endothelium, which can lead to strokes or ischemia. A POSA would have known that the left ventricle of the Fabry patient's heart also becomes very think and leads to myocardial issues, and the nephrons are also affected, leading to kidney issues. A POSA would have known that male Fabry patients typically die in their 40s and 50s. A POSA would have known that oftentimes Fabry Disease is diagnosed by neuropathic pain or corneal warts in the eye, something that can be seen by an optometrist or ophthalmologist. A POSA would have known that most often, Fabry

patients are identified by neuropathic pain which starts to occur in their late teens or early 20s, and it can be so severe, the patients can become suicidal. *See* Trial Tr. Vol. I at 56:11-57:4 (Dr. Medin direct).

37. A POSA would have been aware that protein mutations occur, giving rise to disease, but that some mutant proteins can be stabilized to function more naturally. A POSA would have been familiar with the different types of mutations that give rise to disease, including missense mutations, which are mutations that occur on a position of the amino acid chain, and the amino acid has been changed from one to another, such as mutation I242F, which is a mutation on the 242 site where isoleucine has been changed to phenylene *See* Trial Tr. Vol. I at 57:22-59:22.

38. A POSA would have been familiar with HEK assays, which are assays that utilize human embryonic kidney ("HEK") cells and which were developed in the 1970s by Dr. Frank Graham of McMaster University, who showed POSAs that they could put pieces of DNA in the HEK cells using plasmids that enter the HEK cells easily through a variety of methods with which a POSA would be familiar. POSAs would have known that you can then grow the plasmids for a long time. As of the 1970s a POSA would have known that that you could use an artificial substrate called "four MUG," which the enzyme α-galactosidase A ("α-Gal A"), an assay protein, recognizes and cleans to make a fluorescent substrate that a POSA could read on a fluorometer and you can calculate observations against known standards to determine the level of enzyme activity in the cells being observed. Plasmids were put into the HEK cells in the 1970s. Mutant forms of enzymes were put into HEK cells in the early 1990s. A POSA would have known how to use a HEK assay to identify Fabry mutations, which can be taught to a graduate student in a very short time. HEK cells are the general workhorse cell lines for everyone in the field. *See* Trial Tr. Vol. I at 61:5-63:7; 63:25-64:5.

39. A POSA would have been familiar with the α-Gal A protein and its propensity for mutating from the early 1970s with the discovery of enzyme defects. Cardiac mutations were identified in α-Gal A in the 1980s and other mutations were identified in the 1990s. *See* Trial Tr. Vol. I at 66:5-10.

40. A POSA would have known that "GLP" refers to good laboratory practice, which was something that became standard with the U.S. Food & Drug Administration in 1978. GLP is focused on quality assurance and quality control. It's concerned with laboratory processes, the conditions in which the processes are carried out, how they are planned, how they are performed, monitored, recorded, archived and reported. A POSA would know that GLP was not designed to establish relative merit or correctness. It is instead a quality assurance, quality control method to document experimental conduct. *See* Trial Tr. Vol. I at 66:11-67:14.

41. A POSA would have known of four treatments for Fabry Disease, including enzyme replacement therapy ("ERT"), substrate reduction therapy, molecular chaperone therapy and gene therapy, though only ERT and chaperone therapy currently have FDA approval, and prior to 2017, only ERT had been approved. *See* Trial Tr. Vol. I at 73:5-74:8.

42. A POSA would have known of migalastat, which was first isolated in 1988. (Trial Tr. Vol. I at 74:18-75:1).

43. The Wu reference (DTX-23) was published May 19, 2011, and is prior art to the asserted claims. Wu discusses migalastat using a variety of names and discloses that it is an amino sugar that serves as a chaperone in that it binds and stabilizes α-Gal A increasing total cellular levels. Wu mentions the development of a cell-based assay to identify mutant forms that are responsive to migalastat, which Wu discloses binds to the active site and chaperones α-Gal A into the right location. Wu discloses that migalastat increased α-Gal A activity in 49 of 81 mutant

forms studied, approximately 60%. Wu discloses that missense mutations, which comprise about 60% of the Fabry mutations then known, are often identified as responsive to migalastat. *See* Trial Tr. Vol. I at 76:1-78:4.

44. The Germain reference (DTX-24) was published in 2012 and is prior art to the asserted claims. Germain discusses two Phase II clinical studies using a pharmacological chaperone. Germain shows that you can demonstrate an increase in HEK cells with the corresponding mutant form of the enzyme in the presence of migalastat. In other words, Germain shows migalastat's usefulness as a Fabry treatment and that six out of nine patients studied, each with missense mutations, were shown to be amenable to migalastat. Germain discloses migalastat being dosed in the studies at 150 mg every other day as being well-tolerated and increasing α-Gal A activity resulting in substrate reduction or Gb3 clearance. *See* Trial Tr. Vol. I at 78:19-80:22.

45. The Benjamin 2016 reference (DTX-6) was published in 2016 and is prior art to the asserted claims. Benjamin 2016 discloses two studies evaluating 150 mg migalastat every other day as the dosing regimen. Benjamin 2016 discloses that study participants needed to have amenable mutations, and they were screened using a "preliminary" HEK-Assay. *See* Trial Tr. Vol. I at 80:23-82:14.

46. Benjamin 2016 discloses the existence of the GLP-HEK Assay. *See* Trial Tr. Vol. II at 137:8-18 (Dr. Hopkin).

47. A POSA would have been motivated to combine the teachings of the Wu, Germain and Benjamin 2016 references due to their overlapping subject matter, including that they are focused on migalastat as a pharmacological chaperone treatment for Fabry Disease, and Germain and Benjamin 2016 both point to the same dosing regimen, 150 mg of migalastat every other day. *See* Trial Tr. Vol. I at 95:24-96:10.

48. A POSA would have drawn on their knowledge of HEK Assays, the migalastat amenability criteria disclosed in Wu and the disclosures establishing that about 60% of missense mutations, the same type of mutations claimed in the asserted claims, would be amenable to migalastat, which naturally would have motivated them to evaluate every Fabry patient with a missense mutation for amenability with at least a reasonable likelihood of identifying the mutation as amenable. *See* Trial Tr. Vol. II at 138:17-139:20; 144:22-147:5 (Dr. Hopkin testifying to his practice of ordering HEK Assay testing for mutations not on the Galafold product list).

49. A POSA would have had missense mutations tested even if the specific mutation had been identified elsewhere as nonamenable given how HEK Assays are performed and the variability of amenability criteria. *See* Trial Tr. Vol. I at 88:14-107:12.

50. The '319 publication (JTX-11) was published June 23, 2011, and is prior art to the asserted claims. The '319 publication discloses methods for determining the responsiveness to migalastat in a cell line, noting that at the time over 600 Fabry mutations had been reported, about 60% of which were missense mutations. It refers to migalastat as 1-deoxygalactonojirimycin or "DGJ," and discloses that missense mutations comprise the majority of mutations. *See* Trial Tr. Vol. I at 82:21-85:19.

51. The Lockhart publication (DTX-26) was published in 2015 and is prior art to the asserted claims. It discloses in multiple places the dosing regiment of 150 mg of DGJ hydrochloride, which is 123 mg of the free base migalastat, every other day *See* Trial Tr. Vol. I at 85:20-87:12.

52. A POSA would have been motivated to combine the teachings of the '319 publication and Lockhart publication due to their overlapping subject matter, including that they

are focused on migalastat as a pharmacological chaperone treatment for Fabry Disease. *See* Trial Tr. Vol. I at 96:11-16.

53. APOSA would have drawn on their knowledge of HEK Assays, the migalastat amenability criteria disclosed in the '319 publication and the disclosures establishing that about 60% of missense mutations would be amenable to migalastat, which naturally would have motivated a POSA to evaluate every Fabry patient with a missense mutation for amenability with at least a reasonable likelihood of identifying the mutation as amenable. *See* Trial Tr. Vol. II at 138:17-139:20; 144:22-147:5 (Dr. Hopkin testifying to his practice of ordering HEK Assay testing for mutations not on the Galafold product list).

54. A POSA would have had missense mutations tested even if the specific mutation had been identified elsewhere as nonamenable given how HEK Assays are performed and the variability of amenability criteria. *See* Trial Tr. Vol. I at 84:14-107:12.

Dated: November 5, 2025

Respectfully submitted,

KRATZ & BARRY LLP

/s/ R Touhey Myer
R Touhey Myer (#5939)
800 N. West Street
Wilmington, DE 19801
(302) 527-9378
tmyer@kratzandbarry.com

Of Counsel:

Timothy H. Kratz *(Pro Hac Vice)*
George J. Barry III *(Pro Hac Vice)*
John Thallemer *(Pro Hac Vice)*
KRATZ & BARRY LLP
1050 Crown Point Parkway, Suite 500
Atlanta, GA 30338
(404) 431-6600
tkratz@kratzandbarry.com
gbarry@kratzandbarry.com
jthallemer@kratzandbarry.com

Michael P. Hogan *(Pro Hac Vice)*
KRATZ & BARRY LLP
P.O. Box 63765
622 S. 4th Street
Philadelphia, PA 19147
(917) 216-8585
mhogan@kratzandbarry.com

Attorneys for Defendants,
Aurobindo Pharma Ltd.
and Aurobindo Pharma USA, Inc.